Illinois Department of Public Health
Lysosomal Storage Disorders Subcommittee
Illinois Department of Public Health
Meeting and Conference Call Minutes: April 22, 2015

Subcommittee Members Attending
Joel Charrow, Kitty Keating, Barbara Burton, Lurie Children's Hospital – Chair
Darrel Waggoner, Lainie Friedman-Ross, Maria Helgeson - University of Chicago
George Hoganson- University of Illinois Chicago
Jennifer Burton - University of Illinois Chicago at Peoria
Kathy Grange-Washington University St. Louis Children's Hospital
Michael Schneider- Carle Hospital-Champaign
Brad Tinkle-Advocate Lutheran General Hospital
Brook Croke-Genetic Counselor

IDPH Staff
Khaja Basheeruddin, Rong Shao, George Dizikes, David Culp, Conny Moody, Arthur Kohrman, Claudia Nash, Shannon Harrison, Maria Crain, Rebecca Barnett, Heather Shryock

Guest
Michael Gelb, University of Washington

Background
The meeting was called to order at 4:05 p.m.

IDPH Laboratory Status Report
Khaja Basheeruddin reported that since November 3, 2014, a total of 11,275 samples have been analyzed for five lysosomal storage disorders using tandem mass spectrometry (Fabry, Gaucher, MPS I, Niemann-Pick and Pompe). Thirty-seven newborns were found to have an abnormal screening result, with twenty –five having a presumptive positive result, and twelve with a borderline abnormal result. During this time period, the positive screening rate for Fabry, Gaucher, MPS I and Niemann-Pick ranged from 0.03-0.06%, with the rate for Pompe being somewhat higher. IDPH lab staff are re-evaluating data and will adjust the GAA cutoff to bring the positive screening rate for Pompe in line with the other four disorders.

Currently specimens from only eight hospitals are being screened, but plans are to expand statewide, with screening of all samples received by the IDPH Lab planned for June 1, 2015. Screening for MPS II will be added at a later date. Dr. Gelb indicated the MPS II substrate has been used successfully in his lab, but Perkin Elmer is not yet mass producing it. There was discussion regarding whether MPS II can be multiplexed with the other assays or not. It is believed that a separate bloodspot punch will need to used for the incubation phase, but that it may be possible to combine with the other LSDs for MS/MS analysis.

Data and Case Reviews
Of the 37 newborns found to have an abnormal screening result, all presumptive positive cases were referred and are being seen by a specialist, as recommended and 26 cases have been closed as normal. Eleven cases are still pending, with preliminary findings that suggest one case may be Gaucher and one may be MPSI.

Cases were reviewed, for which parental consent was obtained. The following issues were discussed at length.

MPS I: Follow-up testing for MPS I was discussed. Urine GAGs (glycosaminoglycans) are normally high in the first weeks of life, so it is recommended that testing be delayed until two weeks of age to obtain a valid result. It was also noted that utilizing a lab with experience in testing newborns is suggested, and that only one-third of labs routinely perform fractionation when urine GAGs are ordered.

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Pompe/VUS: The question arose regarding how to determine the timeline and the follow-up protocol for cases with ambiguous molecular results. A Pompe screen- positive case was discussed, which had a slightly reduced confirmatory GAA enzyme level by Mayo laboratories. Clinical exam, chest X-ray and EKG were normal, and molecular testing indicated one pseudodeficiency allele and one variant of unknown significance. Parental testing will be ordered to determine if the mutations were inherited in a cis or trans pattern. After discussion, it was suggested these cases should be followed every three months during the first year of life, then subsequently every six months, and gradually, on an annual basis. The IDPH newborn screening program will categorize these cases as "presumptive positive" and will follow-up annually with the specialist. It was discussed that these scenarios create "patients in waiting" and there will be varying family response to this type of long range monitoring, with some families being anxious and some being unwilling to return. It was discussed that accumulation of data over time, regarding the significance of some of these mutations is the only way to resolve this issue.

Other IDPH Issues

Dr. Kohrman indicated that the IDPH Director, Dr. Nirav Shah, agrees that plans to implement statewide testing for five LSDs should proceed, and that testing for Krabbe will not be implemented until the molecular component is available. A 30 day notice will be sent out to hospitals around May 1st and will also indicate that with the implementation of statewide testing, the fee will be increased $2, from $88 to $90. A provision was made during the last change to the newborn screening legislation that added MPS I and MPS II to the Illinois screening panel, which allowed the fee to be increased $2 for each new LSD added. Since MPS I testing will be implemented June 1st, that is the rationale for the $2 fee increase. Recent legislation provided for the removal of $5 million from the newborn screening fund, and half of that amount has already been swept from the fund.

Adrenoleukodystrophy (ALD): House Bill 2790 is being sponsored by Representative Laura Fine, and would add screening for ALD to the Illinois newborn screening panel. This legislation would require a series of provisions to be in place prior to the implementation of screening. The bill would also raise the base newborn screening fee to $118. This proposed increase would be beneficial since the newborn screening laboratory costs are currently not totally being met by the existing fee, and are being supplemented each year by general revenue funds. With the addition of screening for ALD, an additional fee increase would occur, bringing the total amount to $129. This and all future disorder-specific fee increases would not go into effect until three months prior to the implementation of any new screening test. The Illinois Hospital Association is in agreement with these proposals. HB 2790 has passed out of the House and is now being picked up in the Senate by Senator Dale Righter, sponsor of prior newborn screening legislation.

Guest Presenter Dr. Michael Gelb

Dr. Gelb briefly presented research occurring in his lab to improve the sensitivity of an assay measuring GALC enzyme activity, which would improve the ability to predict disease outcome for newborns identified with Krabbe mutations, and better distinguish between late and early onset forms of the disease. Once Dr. Gelb's lab has completed more testing with specimens from diagnosed adults, the Illinois specialists could submit samples to Dr. Gelb's lab from consented patients referred to them, to assist in providing better information to parents about the anticipated course of the disease in their child.

Other Business

It was reported this week's edition of the Journal of the American Medical Association contains an article about newborn screening.

The next meeting of the LSD Subcommittee will meet May 27th at 4:00 p.m.

Meeting adjourned at 5:03 p.m.